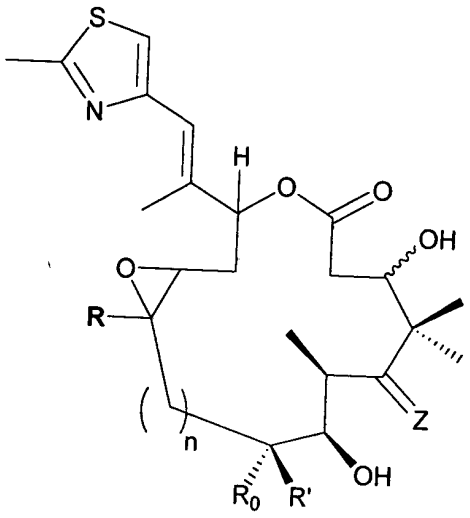
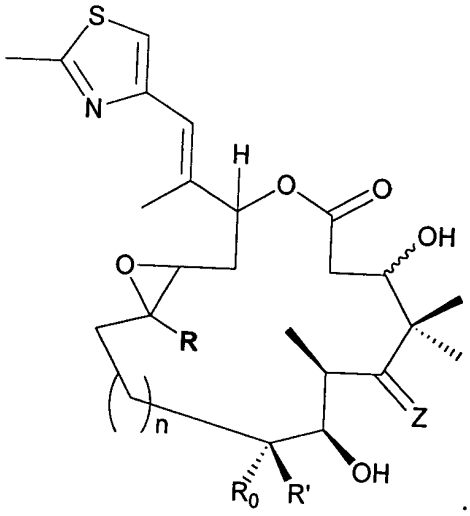
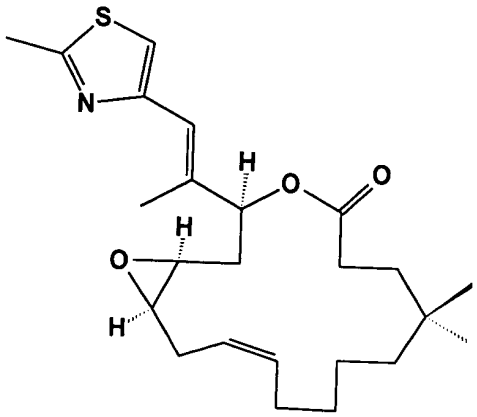
30. (Amended) A pharmaceutical composition for treating cancer comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



;

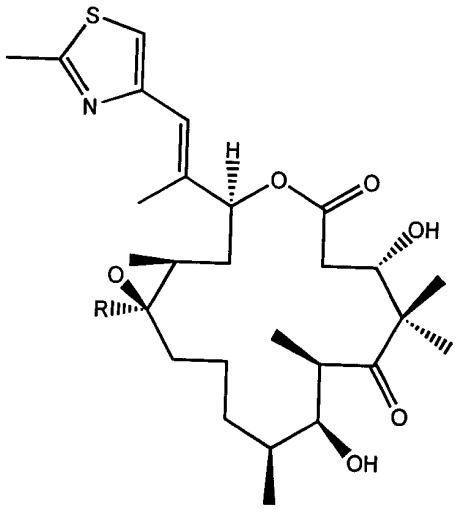


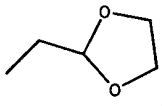
; or



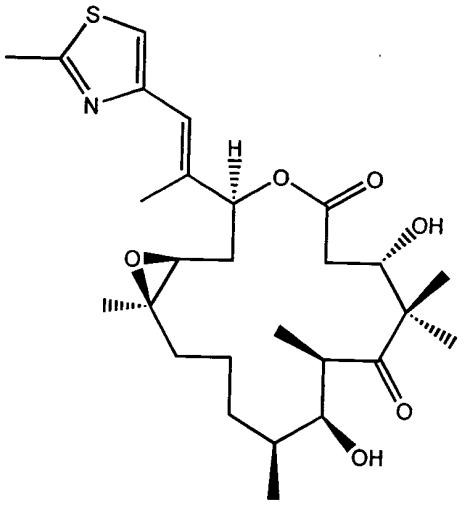
wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

60. (Amended) A pharmaceutical composition comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



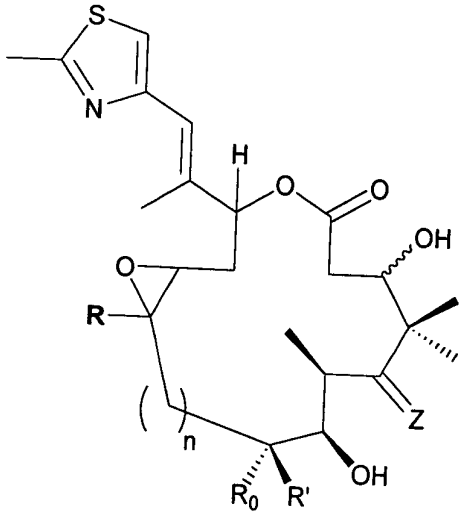
wherein R is hydrogen, methyl, ethyl, n-propyl, n-butyl, n-hexyl, CH_2OH, $(CH_2)_3OH$, or  ; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

69. A pharmaceutical composition comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has [having] the structure:

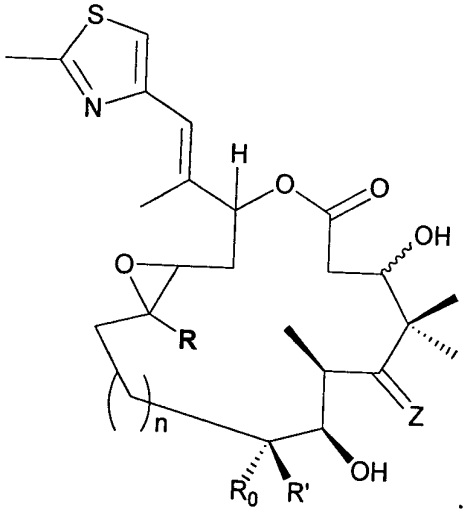


[and a pharmaceutically acceptable carrier]; and
wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

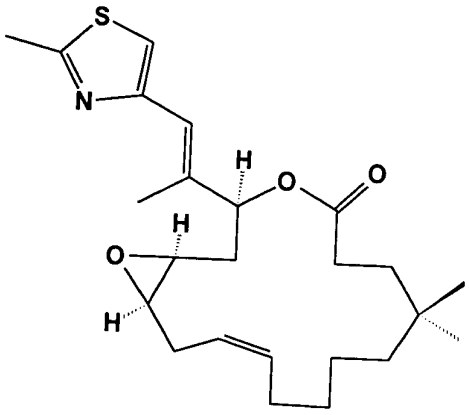
71. (Amended) A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound having the structure:



;



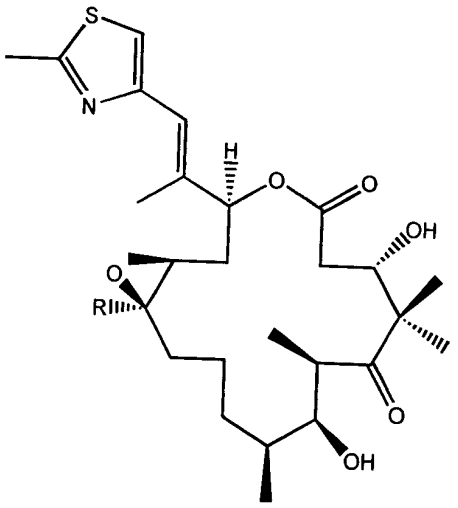
; or

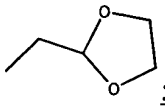


wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally

substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

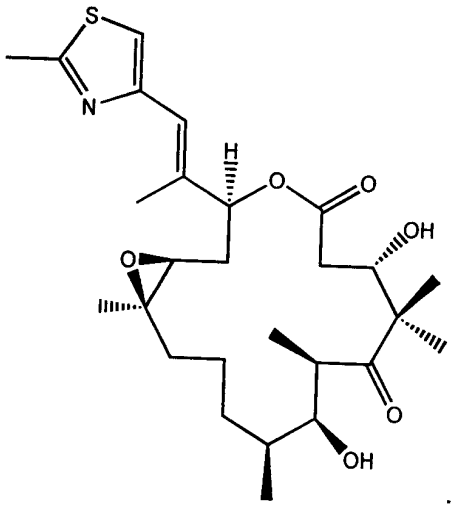
73. (Amended) A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound having the structure:



wherein R is hydrogen, methyl, ethyl, n-propyl, n-butyl, n-hexyl, CH_2OH, $(CH_2)_3OH$, or 

; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

86. (Amended) A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound having the structure:



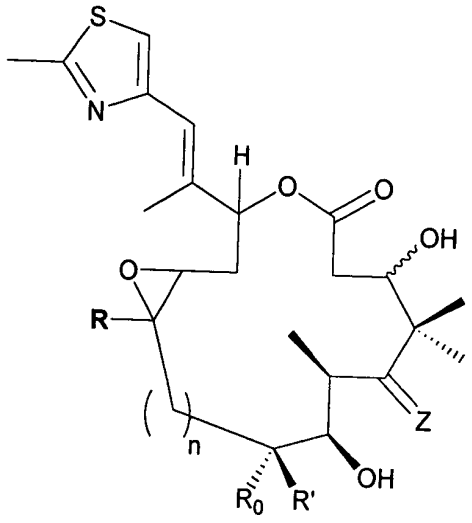
; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

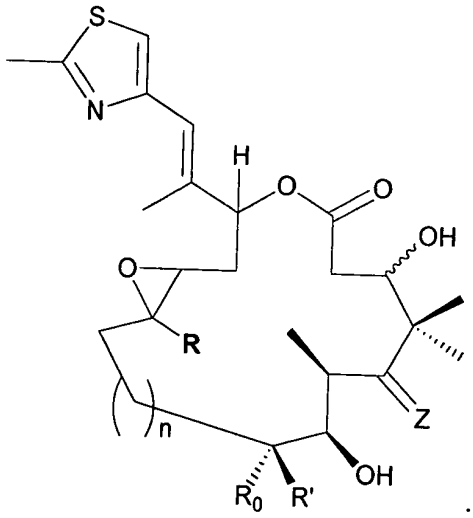
II. Addition of Claims:

Please add the following new claims 95-143:

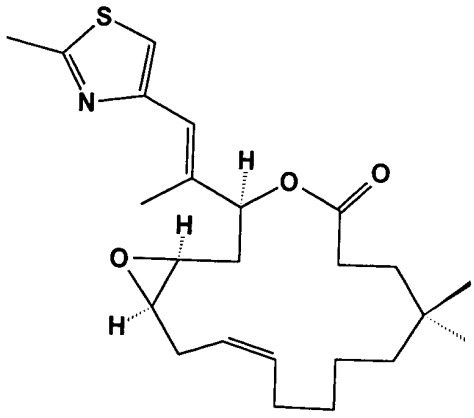
--95. A pharmaceutical composition for the treatment of cancer comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



;



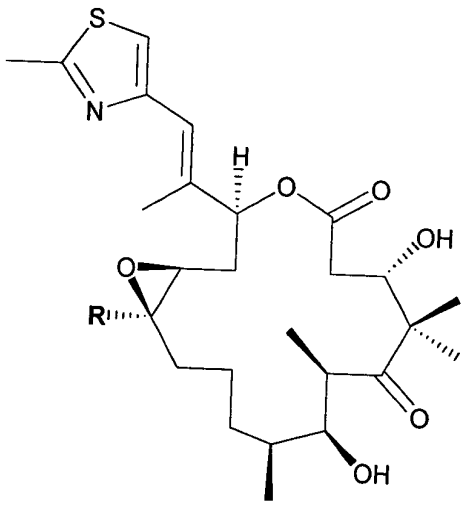
; or



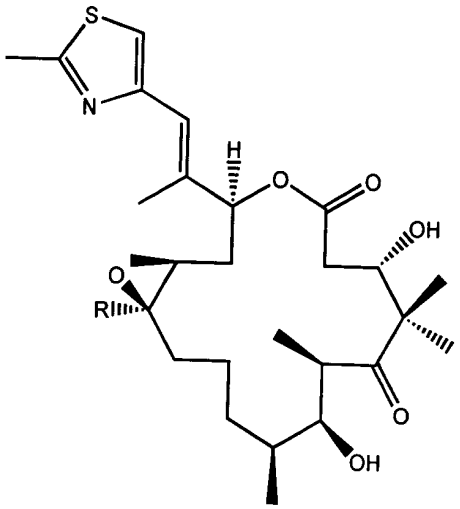
wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally

substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3, and pharmaceutically acceptable salts thereof; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.01 mg to about 25 mg compound per kg body weight of a subject.

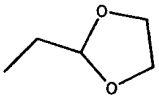
96. The pharmaceutical composition of claim 95, wherein the compound has the structure:



97. A pharmaceutical composition for the treatment of cancer comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



wherein R is hydrogen, methyl, ethyl, n-propyl, n-butyl, n-hexyl, CH_2OH, $(CH_2)_3OH$, or



, and pharmaceutically acceptable salts thereof; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.01 mg to about 25 mg compound per body weight of a subject.

98. The pharmaceutical composition of claim 97, wherein R is hydrogen.

99. The pharmaceutical composition of claim 97, wherein R is ethyl.

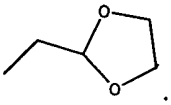
100. The pharmaceutical composition of claim 97, wherein R is propyl.

101. The pharmaceutical composition of claim 97, wherein R is n-butyl.

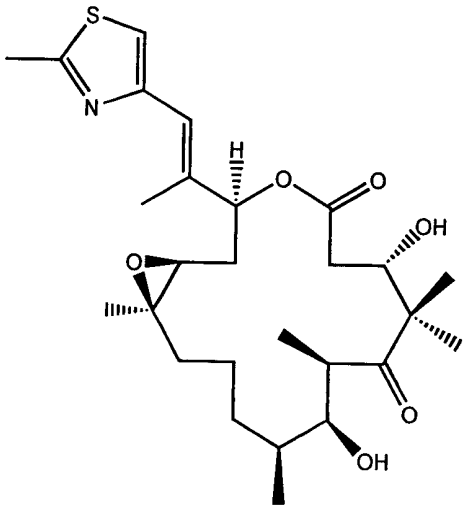
102. The pharmaceutical composition of claim 97, wherein R is n-hexyl.

103. The pharmaceutical composition of claim 97, wherein R is CH_2OH.

104. The pharmaceutical composition of claim 97, wherein R is $(CH_2)_3OH$.

105. The pharmaceutical composition of claim 97, wherein R is  .

106. A pharmaceutical composition for the treatment of cancer comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



and pharmaceutically acceptable salts thereof; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.01 mg to about 25 mg compound per kg body weight of a subject.

107. The pharmaceutical composition of claim 106, further comprising vinblastine.

108. The pharmaceutical composition of claim 106, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.001 mg to about 1 mg compound per kg body weight.

109. The pharmaceutical composition of claim 106, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.01 mg to about 0.6 mg compound per kg body weight.

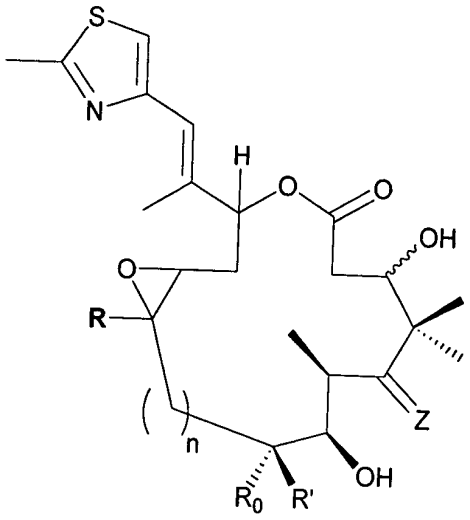
110. The pharmaceutical composition of claim 106, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.01 mg to about 0.3 mg compound per kg body weight.

111. The pharmaceutical composition of claim 106, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.4 mg to about 0.8 mg compound per kg body weight.

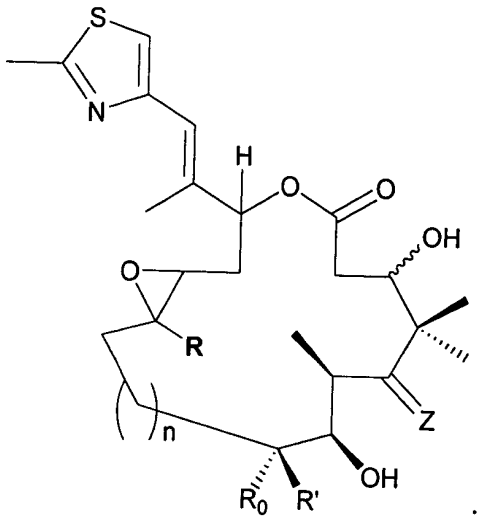
112. The pharmaceutical composition of claim 106, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.3 mg to about 0.6 mg compound per kg body weight.

113. A method of treating cancer in a subject suffering therefrom comprising:

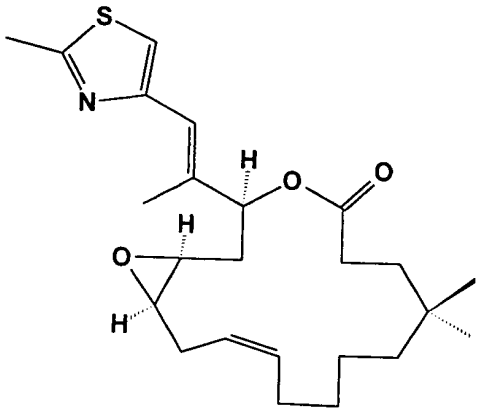
administering to the subject more than one dosage of a therapeutically effective amount of a compound having the structure:



;



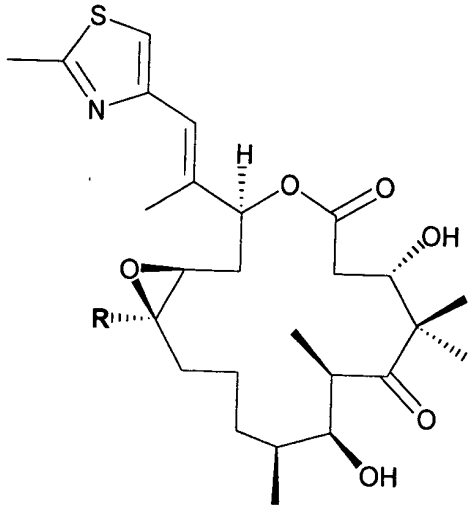
; or



wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3, and pharmaceutically acceptable salts thereof;

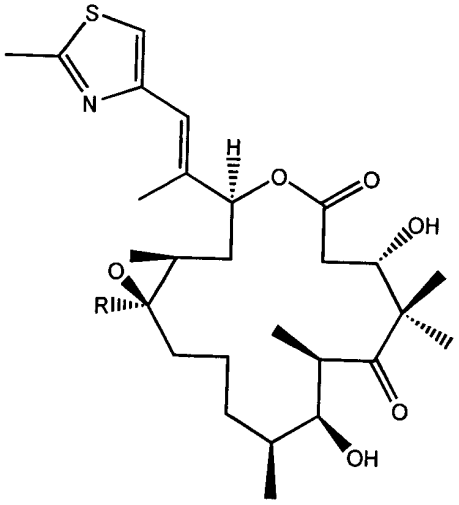
wherein each dosage administration comprises a therapeutically effective amount sufficient to deliver about 0.001 mg to about 25 mg compound per kg body weight.

114. The method of claim 113, wherein the compound administered has the structure:

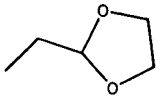


115. A method of treating cancer in a subject suffering therefrom comprising:

administering to the subject more than one dosage of a therapeutically effective amount of a compound having the structure:



wherein R is hydrogen, methyl, ethyl, n-propyl, n-butyl, n-hexyl, CH_2OH, $(CH_2)_3OH$, or



, and pharmaceutically acceptable salts thereof;

wherein each dosage administration comprises a therapeutically effective amount sufficient to deliver about 0.001 mg to about 25 mg compound per kg body weight.

116. The method of claim 115, wherein in the compound R is hydrogen.

117. The method of claim 115, wherein in the compound R is ethyl.

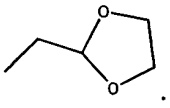
118. The method of claim 115, wherein in the compound R is propyl.

119. The method of claim 115, wherein in the compound R is n-butyl.

120. The method of claim 115, wherein in the compound R is n-hexyl.

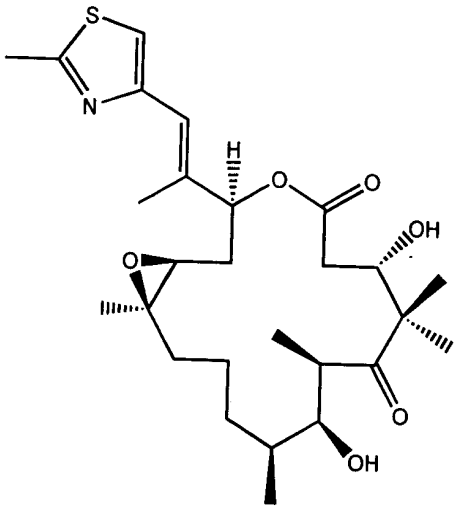
121. The method of claim 115, wherein in the compound R is CH_2OH.

122. The method of claim 115, wherein in the compound R is $(CH_2)_3OH$.

123. The method of claim 115, wherein in the compound R is  .

124. A method of treating cancer in a subject suffering therefrom comprising:

administering to the subject more than one dosage of a therapeutically effective amount of a compound having the structure:



wherein each dosage administration comprises a therapeutically effective amount sufficient to deliver about 0.001 mg to about 25 mg compound per kg body weight.

125. The method of claim 124, wherein the therapeutically effective amount of each dosage administration is an amount sufficient to deliver about 0.001 mg to about 1 mg compound per kg body weight.

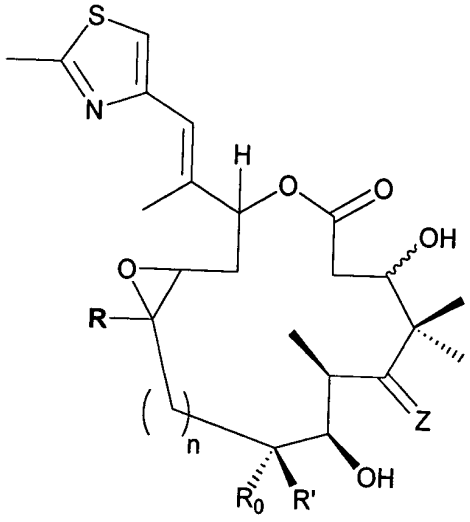
126. The method of claim 124, wherein the therapeutically effective amount of each dosage administration is an amount sufficient to deliver about 0.01 to about 0.6 mg compound per kg body weight.

127. The method of claim 124, wherein the therapeutically effective amount of each dosage administration is an amount sufficient to deliver about 0.01 mg to about 0.3 mg compound per kg body weight.

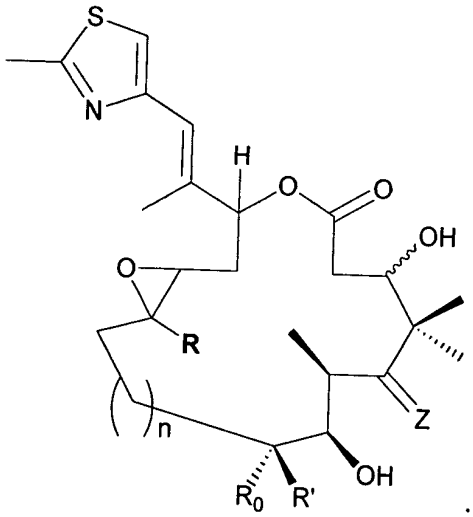
128. The method of claim 124, wherein the therapeutically effective amount of each dosage administration is an amount sufficient to deliver about 0.4 mg to about 0.8 mg compound per kg body weight.

129. The method of claim 124, wherein the therapeutically effective amount of each dosage administration is an amount sufficient to deliver about 0.3 mg to about 0.6 mg compound per kg body weight.

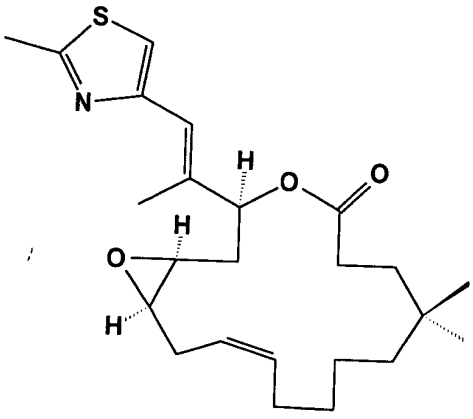
130. A pharmaceutical composition for treating cancer comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



;



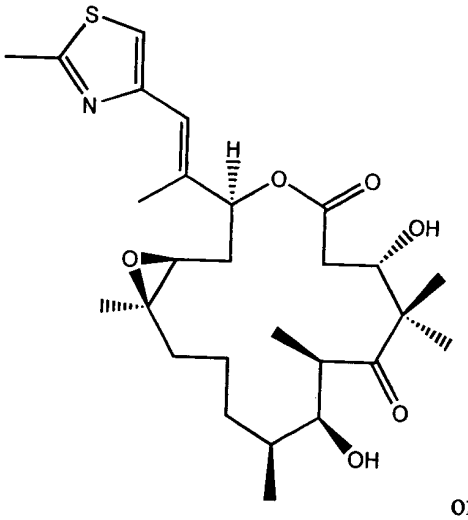
; or



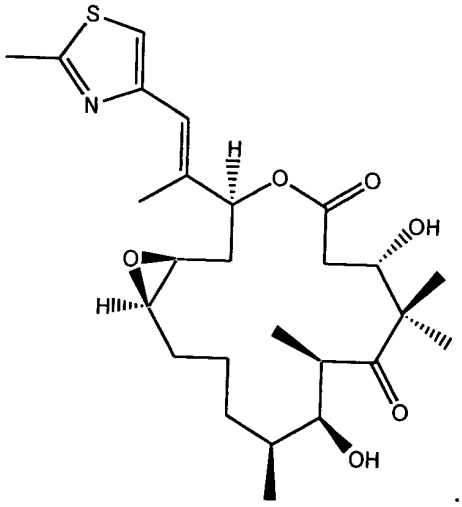
wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally

substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 10 mg compound per kg body weight.

131. A pharmaceutical composition comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:

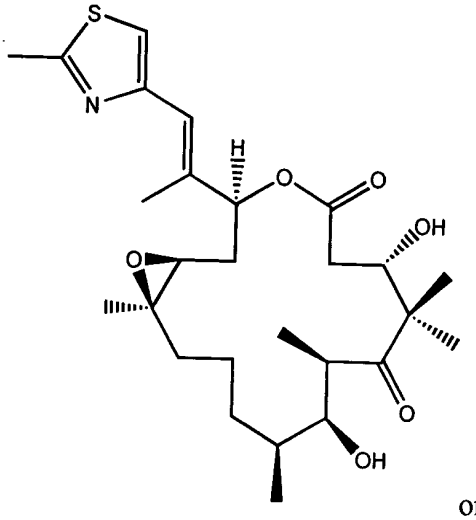


or

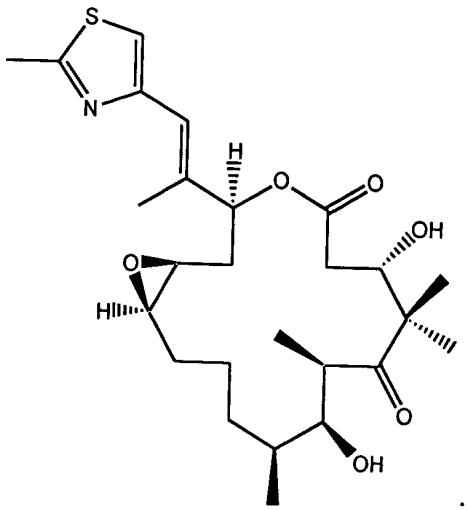


; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

132. A pharmaceutical composition comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



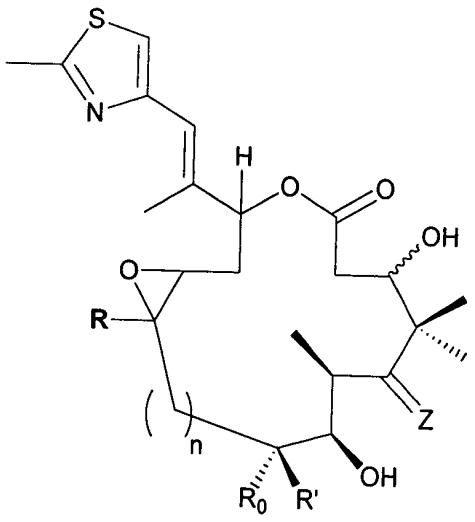
or



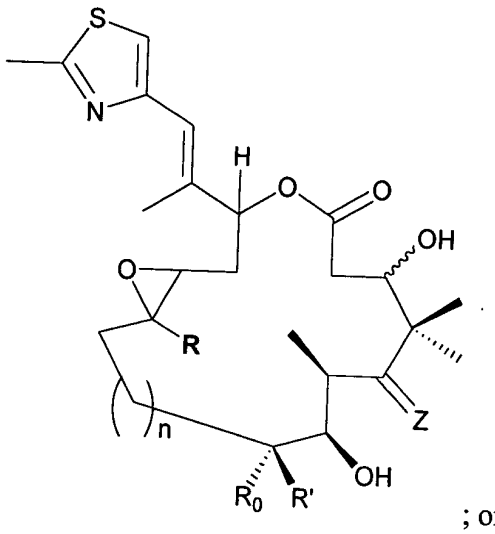
; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 10 mg compound per kg body weight.

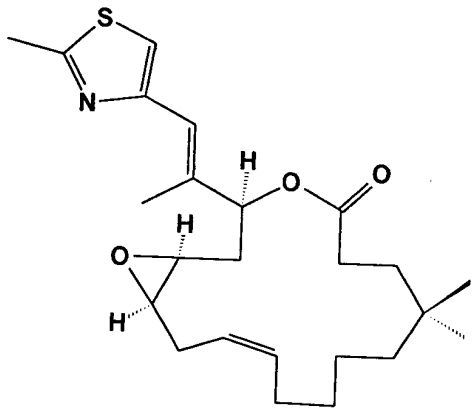
133. A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound having the structure:



;

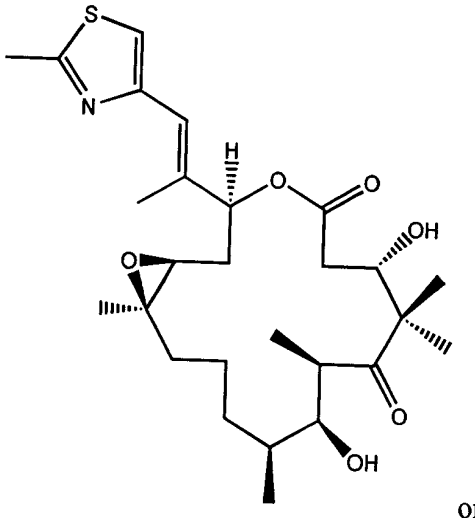


; or

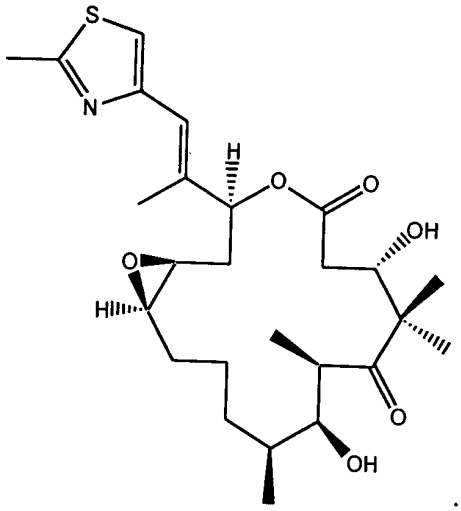


wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is amount sufficient to deliver about 0.001 mg to about 10 mg compound per kg body weight.

134. A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound having the structure:



or

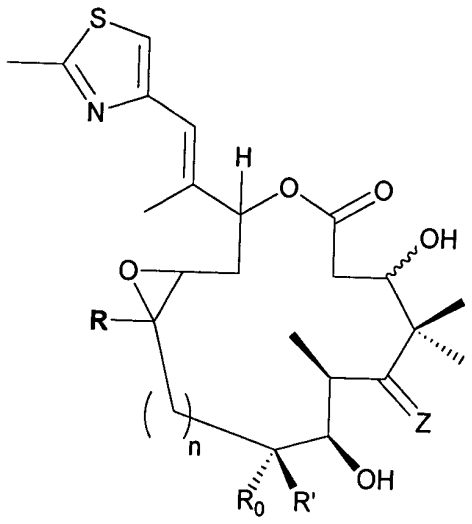


; and

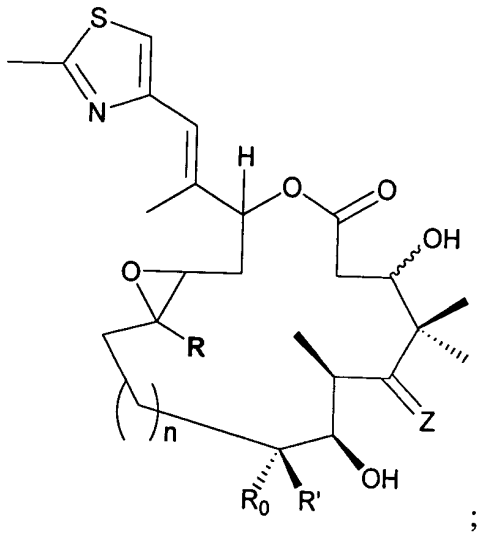
wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

135. The method of claim 71, wherein the step of administering comprises:

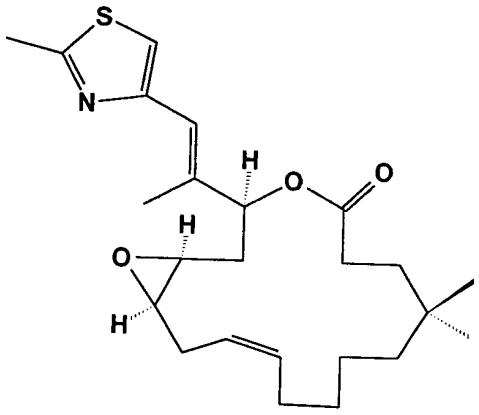
administering to the subject multiple times a therapeutically effective amount of a compound having the structure:



;



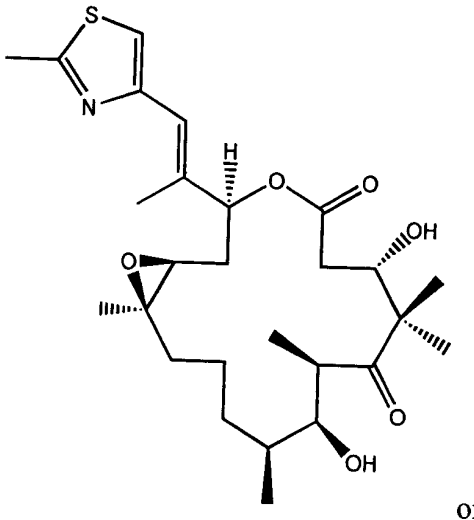
; or



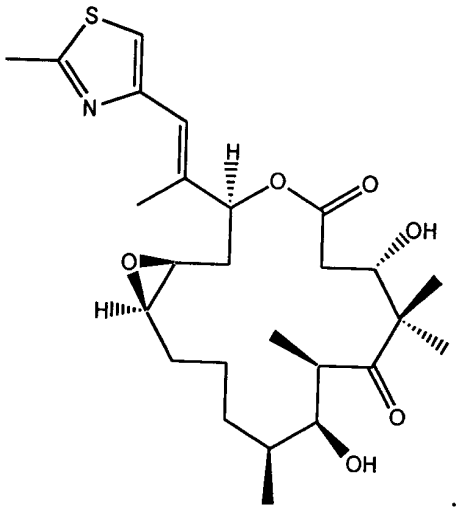
wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is amount sufficient to deliver about 0.001 mg to about 10 mg compound per kg body weight.

136. The method of claim 134, wherein the step of administering comprises:

administering to the subject multiple times a therapeutically effective amount of a compound having the structure:



or

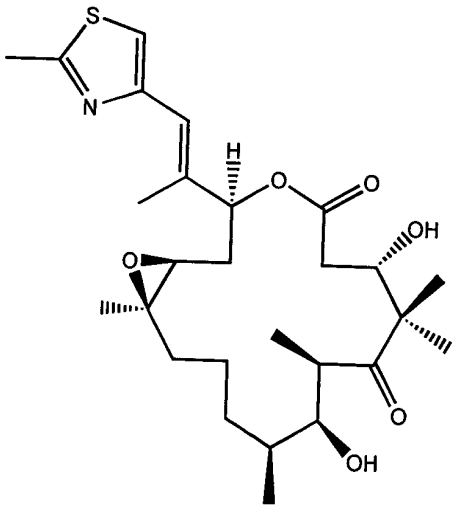


; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

137. The method of claim 124, wherein the step of administering comprises:

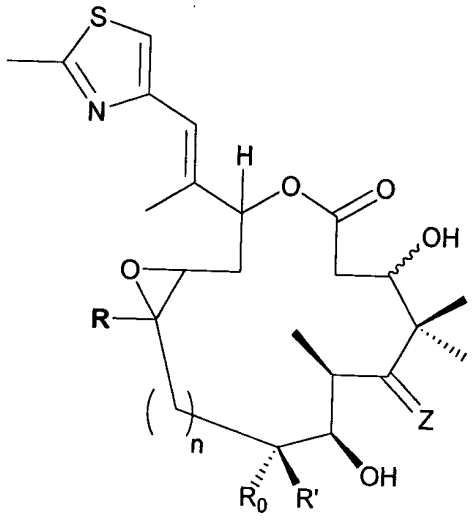
administering to the subject multiple times a therapeutically effective amount of a compound having the structure:



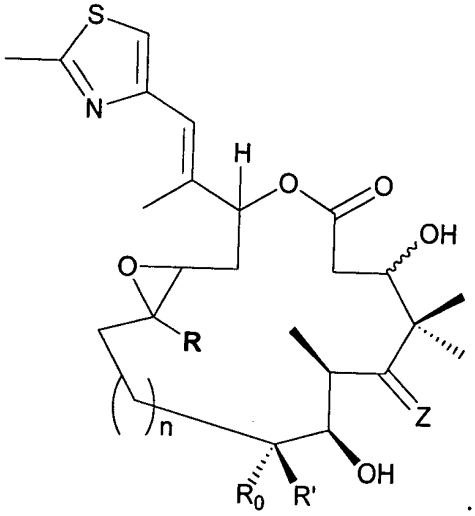
wherein the therapeutically effective amount comprises an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

138. The method of claim 71, wherein the step of administering comprises:

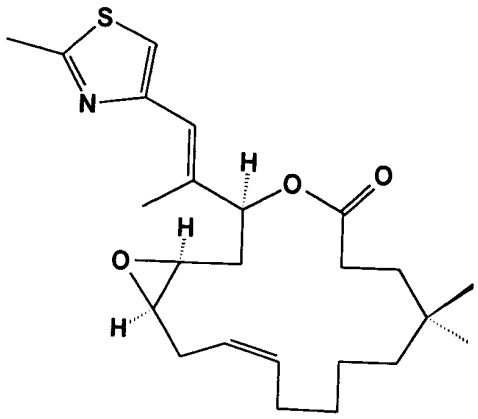
administering to the subject in multiple doses a therapeutically effective amount of a compound having the structure:



;



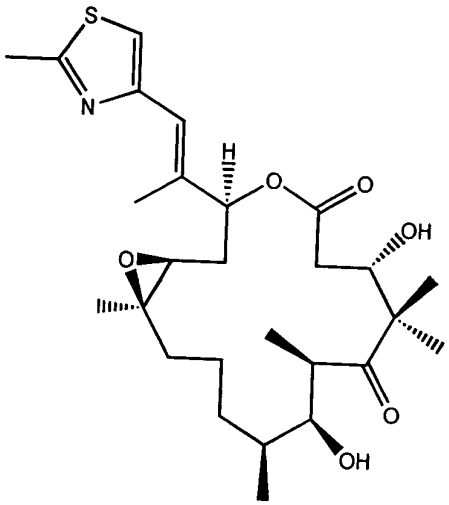
; or



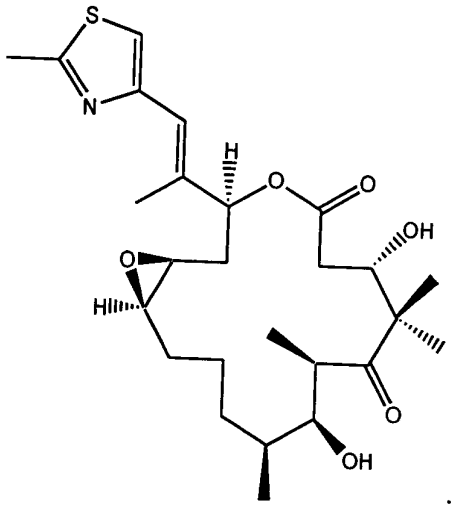
wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is amount sufficient to deliver about 0.001 mg to about 10 mg compound per kg body weight.

139. The method of claim 134, wherein the step of administering comprises:

administering to the subject in multiple doses a therapeutically effective amount of a compound having the structure:



or

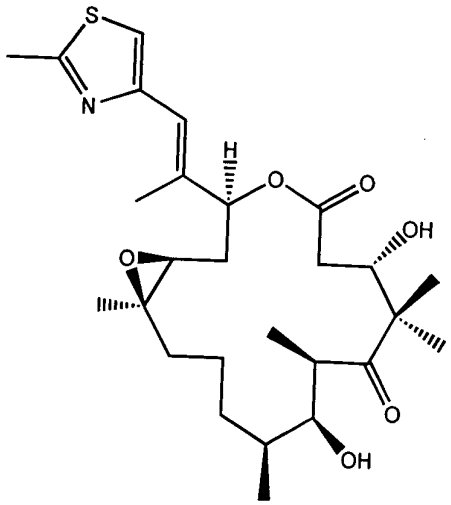


; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

140. The method of claim 124, wherein the step of administering comprises:

administering to the subject in multiple doses a therapeutically effective amount of a compound having the structure:



wherein the therapeutically effective amount comprises an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

141. The composition of claim 30, further comprising at least one additional cytotoxic agent.

142 The composition of claim 139, wherein said at least one additional cytotoxic agent is an anti-cancer agent.

143. The composition of claim 140, wherein the anti-cancer agent is selected from the group consisting of adriamycin, vinblastin, and paclitaxel.--

III. Rejection of claims 30 and 59-94 under 35 U.S.C. § 103(a):

The Examiner has rejected claims 30 and 59-94 under 35 U.S.C. § 103(a) as being unpatentable over the Bollag *et al.* reference (*Cancer Res.*, Vol. 55 (1995), pages 2325-2333). The Examiner asserts that the Bollag *et al.* reference teaches "epothilones A and B, their compositions as an oily residue (column 2, page 2326) and methods of use for treating cancer or tumor cells and particularly multiple drug-resistant cells. (See column 2, page 2331)." The Examiner further asserts that the Bollag *et al.* reference teaches "the method of use of epothilones in combination with taxol (a cytotoxic agent). See column 2, page 2328 to column 1, page 2330." In the section entitled "Ascertainment of the difference between the prior art and the claims" the Examiner states that "the difference between the instant invention and the disclosure of Bollag *et al.*, is that applicants are claiming effective amounts of epothilones from 0.001 to 40 mg/kg of body weight." In the section labeled "Finding of *prima facie* obviousness—rational and motivation" the Examiner then asserts that "for the Bollag *et al.*, to use epothilones for the treatment of cancer or tumors, effective amount must necessarily be used," and states that Applicant's "claiming effective amounts of epothilones from 0.001 to 40 mg/kg of body weight, is not in and of itself patentable over the prior art of Bollag *et al.*" The Examiner further states that "the motivation is to make additional epothilone compositions useful for the treatment of cancer."

Applicant respectfully submits that the Examiner does not establish a *prima facie* case of obviousness based on the Bollag *et al.* reference. In particular, Applicant respectfully submits that the reference by Bollag *et al.* does not teach the preparation or use of compositions

comprising *therapeutically effective amounts* of epothilones in treating cancer. At most, Bollag *et al.* might be said to provide motivation to try to prepare and use such compositions, but there can be no reasonable expectation of success based on the teachings of Bollag *et al.*

The teachings of Bollag *et al.* are very limited. Bollag *et al.* teach epothilones purified from a natural source, *Sorangium cellulosum*, and therefore, are necessarily limited to epothilones A and B, the two epothilones produced by the organism. Bollag *et al.* does not teach or suggest derivitization and modification of the isolated epothilones A and B. By contrast, the present application teaches a variety of different epothilone compounds, and provides a synthetic strategy that, as indicated, allows ready introduction of certain structural variations and derivatization to produce a wide array of epothilones beyond epothilones A and B. Bollag *et al.* does not teach or suggest any such structural variations; its teachings are absolutely limited to epothilones A and B.

Furthermore, because the Bollag *et al.* reference describes the testing of epothilones A and B only in *in vitro* assays (*i.e.*, to evaluate their effects on tubulin polymerization and growth inhibition in cell culture), Bollag *et al.* cannot teach or suggest a pharmaceutical composition comprising a therapeutically effective composition even of epothilones A and B. The reference itself acknowledges that results in such *in vitro* studies often do not correlate with *in vivo* activities (p. 2332, column 2). Bollag *et al.* do not provide any evidence that epothilones A and B will work to inhibit cell growth or kill cells *in vivo* such as in an established animal model for cancer. By contrast, the present application provides evidence in the form of data from well-established mouse models for cancer demonstrating that epothilone B (see tables 8, 12, and 13), as well as other epothilones, are useful in the treatment of cancer. Applicant therefore provided the first demonstration in an established animal cancer model that pharmaceutical compositions comprising a therapeutically effective amount of an epothilone are effective in killing tumor cells and inhibiting the growth of tumor cells. Moreover, Applicant discovered the novel and non-obvious therapeutically effective dose ranges to achieve the desired anti-cancer effect in an animal. The Bollag *et al.* reference does not disclose or suggest the ranges claimed by Applicant and therefore does not provide a basis for rejecting claims containing those ranges under 35 U.S.C. § 103.

Bollag *et al.* particularly fails to teach compositions comprising an amount of epothilone

sufficient to deliver between 0.001 to 40 mg epothilone per kg body weight. Bollag *et al.* only teaches amounts of epothilone A and B useful in mitotic arrest studies (*e.g.*, 10^{-7}-10^{-9} M), cytotoxicity studies (*e.g.*, 10^{-7}-10^{-9} M), and microtubule polymerization studies (*e.g.*, 10^{-6}-10^{-9} M), and Bollag *et al.* do *not* teach amounts useful *in vivo*. With regard to *in vivo* use, Bollag *et al.* even state in their Discussion section that "many agents identified as potent agonists or antagonists of *in vitro* activity in drug screening can prove to have secondary activities that limit their usefulness *in vivo*," (p. 2332, col. 2) thereby acknowledging that their own assays may not be able to identify doses that are effective, since such assays fail to identify side effects or other deficiencies of a composition that are seen when it is tested in a whole organism. In contrast, the present specification, which includes experimental evidence from *in vivo* mouse studies supporting the claimed invention, demonstrates the effectiveness of compositions that deliver amounts of epothilone ranging between 0.001 and 40 mg epothilone per kg body weight (see tables 8-18, pages 75-87), as recited in the present claims.

Furthermore, the Bollag *et al* reference itself actually *teaches away* from the desirability of formulating pharmaceutical compositions from epothilones A or B. The reference indicates that Bollag *et al.* considered epothilones A and B to be lead compounds that, once derivatized, might provide the basis for a therapeutic composition. For instance, in the Introduction to the paper, Bollag *et al.* identify their desire to find a novel class of MT-stabilizing drugs that "*might stimulate* the development of more effective cancer chemotherapeutics with this mechanism of action." (p. 2325, col. 1). Similarly, in the Conclusion section, the authors state "the simpler chemical structure of epothilones may instead provide a *useful lead compound in the quest for a drug* operating by the same mechanism MT-stabilizing mechanism as taxol" (p. 2333, col. 1). These statements indicate that Bollag *et al.* themselves did not consider epothilones A and B to be appropriate components of a pharmaceutical compositions; rather they considered these compounds to be starting points in the pursuit of an appropriate therapeutically effective entity.

The Bollag *et al.* reference therefore specifically teaches away from pharmaceutical compositions, as recited in newly added claims 106, 124, 131, 132 134, 136, 137, 139, 140, which refer to effective amounts of epothilone A (claim 131, 132, 134, 136, 139) or epothilone B (claim 106, 124, 131, 132, 134, 136, 137, 139, 140). Moreover, as discussed above the reference provides no guidance for the development of any other pharmaceutical compositions

encompassed by the present claims. The reference provides no teachings or suggestions of how such compositions should be prepared, and no demonstration that one could reasonably be expected to work.

For all the reasons set forth above, the claimed pharmaceutical compositions and methods of treating cancer cannot be rendered obvious by the limited teachings of Bollag *et al.*

IV. Provisional Double Patenting Rejection:

The Examiner has provisionally rejected claims 30 and 59-94 under 35 U.S.C. § 101 as claiming the same invention as that of claims 59-95 of co-pending application number 10/058,695 (the '695 application).

As stated in MPEP 804, "same invention" means identical subject matter. *See Miller v. Eagle Mfg. Co.* 151 US 186 (1984); *In re Vogel*, 422 F. 2d 438, 164 USPQ 619 (CCPA 1970); and *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957). Applicants respectfully submit that claim 59-94 (in 10/058,695) covers the genus of epothilone compounds, whereas each of the claims of 09/874,514 (claims 30 and 59-94) covers a specific subgenus or species of epothilone compounds. Thus, Applicants respectfully submit that identical subject matter is not defined by both sets of claims and statutory double patenting does not exist.

Furthermore, and soley to expediate allowance of this application, Applicant submits herewith a terminal disclaimer. The terminal disclaimer disclaims any portion of the term of a patent that issues from this application that extends beyond a patent that issues from USSN 10/058,695. Applicant submits that the terminal disclaimer submitted herewith removes any basis for an obviousness-type double patenting rejection based on the latter application.

In view of the remarks provided above, Applicants respectfully request that the provisional statutory double patenting rejection be withdrawn and that the claims be allowed without further delay.

V. Objection to claims 59 and 69:

The Examiner has objected to claims 59 and 69 and states that these claims are duplicates. Applicants respectfully submit that claim 59 is directed to epothilone compounds having a variable R group at the C-12 position, whereas claim 69 is directed to compositions